

Durando, A. describes combination chemotherapy with paclitaxel (T) and epirubicin (E) for metastatic breast cancer.

Osaki, A. describes the use of a combination
5 therapy with mitomycin-C, etoposide, doxifluridine and medroxyprogesterone acetate as second-line therapy for advanced breast cancer.

Description of the Invention

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A method for treating or preventing a neoplasia disorder in a mammal, including a human, in need of such treatment or prevention is provided. The method comprises treating the mammal
15 with a therapeutically effective amount of a combination comprising two or more components, the first component is cyclooxygenase-2 inhibitor, and the additional component or components is optionally selected from (a) an antiangiogenesis
20 agent; (b) an antineoplastic agent; (c) an adjunctive agent; (d) an immunotherapeutic agent; (e) a device; (f) a vaccine; (g) an analgesic agent; and (h) a radiotherapeutic agent; provided that the additional component(s) is other than the
25 cyclooxygenase-2 inhibitor selected as the first component and the matrix metalloproteinase inhibitor selected as the second component.

In one embodiment the combination comprises a cyclooxygenase-2 inhibitor and an antineoplastic agent.

30 Besides being useful for human treatment, the present invention is also useful for veterinary treatment of companion animals, exotic animals and farm

animals, including mammals, rodents, and the like. More preferred animals include horses, dogs, and cats.

The methods and combinations of the present invention may be used for the treatment or prevention of

5 neoplasia disorders including acral lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas,

10 capillary, carcinoids, carcinoma, carcinosarcoma, cavernous, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid

15 adenocarcinoma, ependymal, epitheloid, Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma, glucagonoma, hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatocellular

20 carcinoma, insulinoma, intraepithelial neoplasia, interepithelial squamous cell neoplasia, invasive squamous cell carcinoma, large cell carcinoma, leiomyosarcoma, lentigo maligna melanomas, malignant melanoma, malignant mesothelial tumors, medulloblastoma,

25 medulloepithelioma, melanoma, meningeal, mesothelial, metastatic carcinoma, mucoepidermoid carcinoma, neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, oat cell carcinoma, oligodendroglial, osteosarcoma, pancreatic polypeptide, papillary serous

30 adenocarcinoma, pineal cell, pituitary tumors, plasmacytoma, pseudosarcoma, pulmonary blastoma, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma,

sarcoma, serous carcinoma, small cell carcinoma, soft tissue carcinomas, somatostatin-secreting tumor, squamous carcinoma, squamous cell carcinoma, submesothelial, superficial spreading melanoma, undifferentiated carcinoma, uveal melanoma, verrucous carcinoma, vipoma, well differentiated carcinoma, and Wilm's tumor.

The methods and combinations of the present invention provide one or more benefits. Combinations of COX-2 inhibitors with the compounds, compositions, agents and therapies of the present invention are useful in treating and preventing neoplasia disorders. Preferably, the COX-2 inhibitors and the compounds, compositions, agents and therapies of the present invention are administered in combination at a low dose, that is, at a dose lower than has been conventionally used in clinical situations.

A benefit of lowering the dose of the compounds, compositions, agents and therapies of the present invention administered to a mammal includes a decrease in the incidence of adverse effects associated with higher dosages. For example, by the lowering the dosage of a chemotherapeutic agent such as methotrexate, a reduction in the frequency and the severity of nausea and vomiting will result when compared to that observed at higher dosages. Similar benefits are contemplated for the compounds, compositions, agents and therapies in combination with the COX-2 inhibitors of the present invention.

By lowering the incidence of adverse effects, an improvement in the quality of life of a patient undergoing treatment for cancer is contemplated.